REMARKS

It is noted at the outset that a complete claims listing has not been presented with this request for reconsideration. According to current PTO claims amendment practice, a complete claims listing is required only when changes are made to any claims. See, http://www.uspto.gov/web/offices/pac/dapp/revised121gnas.htm.

A final rejection was issued April 19, 2006 in the above-identified patent application. Claims 1-3 and 5-12 stand rejected under 35 USC §103(a) as allegedly unpatentable over U.S. Patent 6,284,539 to Bowen, et al. (Bowen), in view of Takeshima et al., Neuroscience, 60 (3): 809-823(1994) (Takeshima) for the reasons of record in the official action dated July 29, 2005.

A Request for Reconsideration, filed August 21, 2006 was denied in the Advisory Action issued September 13, 2006.

A Notice of Appeal, together with a Pre-Appeal Brief Request For Review was filed October 19, 2006. A Notice of Panel Decision From Pre-Appeal Brief Review (Notice of Panel Decision) was issued November 29, 2006, maintaining the rejections of claims 1-3 and 5-12.

The Notice of Panel Decision stated that the "time period for filing an appeal brief will be reset to be one month from mailing this decision, or the balance of the two-month time period running from the receipt of the Notice of Appeal, whichever is greater". The unextended due date for filing an Appeal Brief, therefore, was December 29, 2006. A petition for a five month extension of the response period is presented with this submission under 37 C.F.R. §1.114(d), which is being filed before the expiration of the five month extension period.

By way of review, the finally rejected claims are drawn to a method of inducing a dopaminergic neuronal fate in a neural stem cell or neural progenitor cell. The claimed method calls for particular treatments to be performed on a neural stem cell or neural progenitor cell. The treatments are:

(i) expressing Nurr1 above basal levels within the cell; and

(ii) co-culturing with a Type 1 astrocyte of the ventral mesencephalon, thereby contacting the cell in vitro with one or more factors secreted from the astrocyte.

The thrust of applicant's argument in the aforementioned Pre-Appeal Brief Request for Review was the Examiner's failure to satisfy the criteria for establishing prima facie obviousness, according to §706.02(j) of the Manual of Patent Examining Procedure. These criteria were based on decisions of the Court of Appeals for the Federal Circuit, including In re Vaeck, 20 USPQ2nd 1438 (Fed. Cir. 1991), involving application of the so-called teaching, suggestion, motivation (or TSM) test for non-obviousness.

In the meantime, the appropriate framework for determining non-obviousness under 37 USC §103(a) was reviewed by the U.S. Supreme Court in KSR International Co. v Teleflex Inc., S.Ct. 2007 WL1237837 (U.S.). In that case, the Supreme Court stated that obviousness should not be determined by means of ridgely applied criteria in the manner that the Federal Circuit had done in developing the TMS test. The opinion in
KSR made it clear that the TMS test was simply one approach that may be followed in assessing non-obviousness under §103. The Supreme Court hastened to add that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant filed to combine the [prior art] elements" in the manner claimed. In this connection the Court stated:

> "Often, it will be necessary... to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the market place; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent as issue. To facilitate review, this analysis should be make explicit. KSR, slip op, at 14 (emphesis added).

In view of the above-quoted statement from KSR, the U.S. Patent and Trademark Office released a memorandum instructing examiner's that, in formulating a rejection under 35 USC §103(a), based upon a combination of prior art elements, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed". See May 3, 2007 memo of M.A. Focarino, Deputy Commissioner for Patent Operations.

In the present case, the Examiner has failed to identify any plausible reason why a person of ordinary skill in the art would have combined elements of Bowen and Takeshima in the matter

claimed by applicants herein.

Neither Bowen or Takeshima describes culturing a neural stem cell or neural progenitor cell with an astrocyte of the ventral mesencephalon. Neither reference individually or in combination can, therefore, possibly render obviousness the claimed invention, involving treatment of a neural stem cell or neural progenitor cell as claimed.

Bowen describes only a method for generating dopaminergic cells by the induction and endogenous expression in CNS stem cells of a gene coding for the nuclear receptor Nurr1 in order to direct such neuronal precursors to a dopaminergic cell fate which is verified by expression of tyrosine hydroxylase. See the abstract and examples 1 and 2 of Bowen. In the background section, Bowen discloses that co-culturing dopaminergic neurons with striatal astrocytes or with conditioned media from striatal astrocytes has been shown to increase the survival of the neurons. See column 3, lines 11-25 of Bowen.

Takeshima is cited as purportedly providing the reason why a person skilled in the art would have arrived at the combination of the reference disclosures in the manner proposed by the Examiner. However, the Examiner's reliance on Takeshima for this purpose is plainly misplaced. There is no mention of neuronal stem cells or neural progenitor cells in Takeshima. Indeed, the term "development of TH^+ neruons", as used in Takeshima, when properly considered in context, does not include neural stem cells or neural progenitor cells. Rather, the "development of TH^+ neurons" is properly interpreted as the maturation of the neurons, and not inducement of neuronal fate, as presently claimed. Takeshima refers, at page 816, under the heading "Discussion", to "three distinct phases of development" and at page 817 to "the distinct phases of development identified in this study". These phases of development are (I) a progressive neurite development phase; (ii) an adverse growth phase; and (iii) a surge of neuritic growth phase as illustrated, in part, in Figure 5 of Takeshima. These are phases of development of cells already committed to a neuronal fate. Considering the limited context of "development" discussed in this reference, there is no factual basis provided in Takeshima for extrapolating the term "development of TH^+ neurons", so as to include neural stem cells or neural progenitor cells.

The Supreme Court in KSR stated unequivocally that its prior opinion in Graham v. John Deere Co. 383 US 1 (1996) continues to define the inquiry that controls the non-obviousness

analysis under §103. In so stating, the Court reaffirmed the impermissibility of utilizing hindsight in assessing non-obviousness. However, it is apparent that this is precisely what the Examiner has done in the present case. How else can the Examiner's reliance on Takeshima be explained, when Takeshima neither treated the cells that are actually subject to the present invention, i.e. neural stem and progenitor cells, nor observed the result claimed, i.e. induction of a dopaminergic neuronal fate. Takeshima describes the results of an investigation of astrocyte-dependent and astrocyte-independent phases of development and survival of neurons from the medial, ventral mesencephalon of the E14 rat in culture. The purpose of the investigation was to test the hypothesis that dopaminergic neurons were uniquely sensitive to factors produced by Type-1 astrocytes. The ultimate goal of this line of investigation, according to the authors, was to identify endogenous dopaminergic neurotrophic factors (NTF) that might be useful in treating Parkinson's disease. See page 810 of Takeshima . The investigation showed that when grown in a serum-supplemented medium with proliferating glia, the percentage of TH^+ neurons in the culture increased from an initial value of 20%, at 12 hours after plating , to 60% by the 21st day in culture. The authors concluded that an astrocyte-derived NTF that is relatively specific for promoting the survival of the dopaminergic neuronal phenotype is believed to mediate the observed effect.

One of ordinary skill in the art would search Bowen and Takeshima in vain for any reason, much less a technically plausible reason, for attempting to treat different cells to achieve a different result. Indeed, neither Bowen nor Takeshima contains the slightest suggestion to use what is disclosed in one reference in combination with what is disclosed in the other reference. Cf. In re Avery, 186 USPQ 161 (CCPA 1975). That being the case, it cannot reasonably be maintained that the combined disclosures of Bowen and Takeshima fairly suggest doing what the applicants have done. Accordingly, the rejection of claims 1-3 and 5-12 under 35 USC §103(a) based on the combination of these two references is improper. Ex parte Stauber, 208 USPQ 945 (Bd Apps. 1980).

In summary, viewed objectively, and without benefit of applicants' disclosure, the conclusion is inescapable that the combined disclosures of Bowen and Takeshima fail to render applicants' claimed invention prima facie obvious.

In view of the foregoing remarks, it is respectfully requested that the rejection set forth in the April 19, 2006 official action be withdrawn and that this application be passed to issue and such action is earnestly solicited.

Respectfully submitted,
DANN DORFMAN HERRELL and SKILLMAN, P.C.
Attorneys for Applicant

By 
Kathleen D. Rigaut, Ph.D., J.D.
Registration No. 43,047